

1 **Understanding Social Media Discourse on Antidepressants: Unsupervised and**
2 **Sentiment Analysis using X**

3

4 **Short title:** Social Media Discourse of Antidepressants on X

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44 **ABSTRACT**

45 **Background**

46 Antidepressants are essential in managing depression, including treatment-resistant cases.
47 Public perceptions of these medications, shaped by social media platforms like X
48 (formerly Twitter), can influence treatment adherence and outcomes. This study explores
49 public attitudes towards antidepressants through sentiment and topic modeling analysis
50 of tweets in English and Spanish from 2007 to 2022.

51 **Methods**

52 Tweets mentioning antidepressants approved for depression were collected. The analysis
53 focused on selective serotonin reuptake inhibitors (SSRIs) and glutamatergic drugs.
54 Sentiment analysis and topic modeling were conducted to identify trends, concerns, and
55 emotions in discussions across both languages.

56 **Results**

57 A total of 1,448,674 tweets were analyzed (1,013,128 in English and 435,546 in Spanish).
58 SSRIs were the most mentioned antidepressants (27.9% in English, 58.91% in Spanish).
59 Pricing and availability were key concerns in English tweets, while Spanish tweets
60 highlighted availability, efficacy, and sexual side effects. Glutamatergic drugs, especially
61 esketamine, gained attention (15.61% in English, 25.23% in Spanish), evoking emotions
62 such as fear, sadness, and anger. Temporal analysis showed significant increases in
63 discussions, with peaks in 2012 and 2021 for SSRIs in Spanish, and exponential growth
64 from 2018 to 2021 for glutamatergic drugs. Emotional tones varied across languages,
65 reflecting cultural differences.

66 **Conclusions**

67 Social media platforms like X provide valuable insights into public perceptions of
68 antidepressants, highlighting cultural variations in attitudes. Understanding these

69 perceptions can help clinicians address concerns and misconceptions, fostering informed
70 treatment decisions. The limitations of social media data call for careful interpretation,
71 emphasizing the need for continued research to improve pharmacovigilance and public
72 health strategies.

73

74 **Keywords:** Antidepressants; Twitter (X); Selective serotonin reuptake inhibitors (SSRIs);
75 Esketamine; Sentiment analysis.

76 INTRODUCTION

77 Depression is a highly prevalent disorder, being a leading cause of mortality, disability,
78 and reduced quality of life worldwide [1–4]. Depressive symptoms vary widely, and they
79 can be expressed in different intensities and forms. Some of depression’s core symptoms
80 include sadness, anhedonia, guilt, low self-esteem, sleep and eating disturbances, fatigue,
81 impaired concentration, suicidal ideation and suicide attempts [5,6]. The age of onset is
82 around the mid-20s, but symptoms may be expressed earlier during childhood and
83 adolescence [7]. By 2030, depressive disorders are expected to be the largest cause of
84 disease burden [8].

85 Antidepressants are a heterogeneous group of drugs primarily indicated for the treatment
86 of depressive disorders, having demonstrated their effectiveness in this area [9–12].
87 Additionally, these drugs are used in other disorders, such as anxiety, and even in other
88 non-psychiatric conditions, like the treatment of pain or urological diseases [13–15]. In
89 recent years, the global consumption of antidepressants has increased significantly, being
90 the fastest-growing group of psychotropic drugs, with an average annual growth of 3.5%
91 worldwide [9,10,16–18]. Selective serotonin reuptake inhibitors (SSRIs) are among the
92 most used pharmacological treatments and are the first-line therapy for most depressive
93 and anxiety disorders. By 2019, the use of SSRIs had doubled that of all other
94 antidepressants combined, especially in developed countries like the United States and
95 across Europe [1]. Alongside SSRIs, other antidepressants, such as serotonin-
96 norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCA), and
97 glutamatergic modulators, remain alternative therapeutic options [15]. However, recent
98 controversies have considered that the improvements seen in clinical trials may not fully
99 justify their widespread use [19–21]. Concerns about overprescription, long-term side
100 effects such as sexual dysfunction [22,23], have garnered increasing attention.

101 These limitations —such as limited efficacy, significant side effects, and concerns over
102 overprescription— become even more critical in cases of treatment-resistant depression
103 (TRD), a severe form of depression defined as a failure to respond to two or more
104 antidepressant regimens despite adequate dose, duration, and treatment adherence [24].
105 Some authors advocate for the alternative term "difficult-to-treat depression," as TRD
106 underscores the inherent limitations of traditional antidepressants in terms of efficacy
107 [25]. TRD affects approximately 28% of people who suffer from depression, leading to
108 an even higher significant loss of quality of life and functionality [26]. However, the
109 literature claims that there are still many difficulties to address regarding the definition
110 and consequences of TRD, representing an important barrier in mechanistic and
111 translational research [27]. Incorporating TRD as a central topic in the broader discussion
112 of depression treatment is essential to reflect clinical realities and to adapt therapies to the
113 individual characteristics of patients.

114 In this complex landscape, intranasal administration of the glutamatergic modulator
115 esketamine has arisen as a promising agent in the medical management of TRD [15].
116 However, these new treatments come with economic implications and challenges in terms
117 of access, as the high costs and the need for specialized administration limit their
118 availability to broader populations. The rise of precision medicine and personalized
119 therapies [28] offers a shift toward more tailored approaches to TRD, but addressing
120 disparities in access and affordability is crucial to ensure these advancements reach a
121 broader population.

122 Despite the widespread use of antidepressants, negative opinions are still common,
123 leading many patients to hesitate before starting treatment, or becoming non-adherent to
124 the prescription during the treatment period. Although 66% of patients had positive views
125 of antidepressants, they are worried about the doses and safety [6]. This reluctance is

126 often driven by negative beliefs and attitudes toward these medications [29,30].
127 Traditional methods for studying patient experiences, such as surveys and interviews [31–
128 33], may not capture true sentiments due to desirability bias, where patients tend to
129 present themselves more favorably [34]. As a result, patients may avoid sharing negative
130 views about medications in clinical settings, preferring informal spaces like social media
131 to express their true concerns [35–37].

132 Social media offers significant benefits, including access to real-time data, a greater
133 diversity of opinions, and the ability to capture a more accurate picture of social
134 perception [38–40]. Research has demonstrated its effectiveness in identifying adverse
135 events and continuous monitoring of medication use [41–45]. X, as a pharmacovigilance
136 tool for detecting adverse events, has gained relevance in recent years, especially in
137 mental health, where its use as a research vehicle is increasing [46,47]. Previous studies
138 have analyzed changes in X use, identifying increased posting frequency or altered
139 patterns during depressive episodes [48,49], reinforcing the suitability of social media for
140 studying depression-related behaviors. Studies on the use of psychotropic drugs,
141 psychological therapies, and electroconvulsive therapy have found that descriptions on
142 X, as well as the associated social perceptions and emotions, closely resemble scientific
143 evidence, allowing us a better understanding of public perceptions of different therapeutic
144 approaches in mental health [41,50,51]. However, social media algorithms tend to
145 prioritize content with high engagement, which can amplify negative or extreme views,
146 especially about antidepressants, potentially distorting public perception and
147 complicating efforts to promote balanced, evidence-based information.

148 Although some initial studies have evaluated different perspectives and points related to
149 antidepressants on X [50,52], the broader social perspectives, especially cross-cultural
150 and multilingual insights, remain understudied. Social and cultural attitudes play a critical

151 role in shaping public perception, adherence, and overall effectiveness of antidepressant
152 treatments, yet there is a notable gap in research examining these factors across diverse
153 linguistic and cultural contexts. This study uniquely tries to address this gap by applying
154 advanced artificial intelligence techniques to analyze public discussions on X in both
155 English and Spanish. By doing so, we aim to shed light on the social and cultural factors
156 that influence the effectiveness of pharmacological treatment for depression.

157 **METHODS**

158 **X Data Collection Search Strategy**

159 This study focuses on analysing tweets related to antidepressants approved for the
160 treatment of depression and TRD. We employed the *Twitter Binder* search engine to
161 collect all public tweets referencing antidepressant medications approved by the Food and
162 Drug Administration (FDA) or the Spanish Agency of Medicines and Medical Devices
163 (AEM) from January 1, 2007, to December 31, 2022. The search covered tweets in both
164 English and Spanish.

165 The search strategy included both generic drug names and brand names. A full list of the
166 keywords used can be found in the Supplementary Material. The inclusion criteria for the
167 tweets were: a) They must be public, b) They must contain at least one of the listed
168 keywords, c) They must be written in either English or Spanish, and d) Published between
169 2007 and 2022.

170 Due to the relatively limited volume of Spanish tweets mentioning dual agents, other
171 antidepressants, and tricyclics, the analysis was primarily concentrated on the two groups
172 with the highest tweet volumes across both languages: SSRIs and glutamatergic drugs.
173 This allowed for a more focused and robust comparative analysis between the two most
174 frequently discussed groups of antidepressants

175 Content Analysis Process

176 This study applies an unsupervised learning approach named topic modeling to detect
177 groups of tweets inside the Spanish and English databases. After thoroughly revising the
178 available unsupervised methodologies, Latent Dirichlet Allocation (LDA) was selected
179 due to its widespread use, interpretability, and extensive application in X datasets within
180 the literature [53–55].

181 Before applying the unsupervised algorithm, text preprocessing was essential to ensure
182 an optimal model performance. The first step involved separating Spanish tweets from
183 English tweets, allowing LDA to be applied independently to each dataset. Then, tweets
184 in each dataset are refined by removing stopwords, duplicate terms, and non-standard
185 characters such as emojis or hashtags.

186 Determining the number of topics in each dataset was crucial before implementing LDA.
187 A Cluster Validity Index (CVI) was employed to identify the optimal number of topics.
188 CVIs are metrics used in unsupervised learning to assess the effectiveness of clustering
189 by evaluating the arrangement of data points [56]. In this research, the Silhouette
190 Coefficient [56] was the CVI selected due to its ability to measure inter-cluster and intra-
191 cluster distances. For each dataset, we ran LDA five times with the number of topics
192 ranging from 2 to 10. We then calculated the mean Silhouette Coefficient for each topic
193 number across the five iterations and selected the number of topics with the highest mean
194 score [57,58]. With the optimal number of topics identified, we applied LDA to both the
195 Spanish and English datasets. Finally, using LDA, we extracted the most relevant words
196 for each topic, which allowed us to identify the theme and assign an appropriate name to
197 each topic based on these key terms.

198 In the final stage, emotion detection was conducted using a model from Hugging Face's
199 machine learning platform, specifically the "Emotion English DistilRoBERTa-base"

200 model [59] for the English dataset. This model is considered state-of-the-art for detecting
201 Ekman's six basic emotions—anger, disgust, fear, joy, sadness, and surprise—along with
202 the neutral emotion [60]. It has demonstrated an accuracy of 66%, significantly surpassing
203 the 14% probability of random chance (1/7). For the Spanish tweets, we used the
204 Robertuito model [61], which achieved an accuracy of 58%. Both models are built on the
205 RoBERTa architecture; however, DistilRoBERTa employs a distilled version to reduce
206 complexity, while Robertuito uses a full RoBERTa model with 12 self-attention layers,
207 12 attention heads, and a hidden size of 768 to replicate the structure of BERTweet. Both
208 models were pre-trained to classify the emotions of interest, so no additional training was
209 required.

210 **Ethical Aspects**

211 This study was approved by the Research Ethics Committee of the University of Alcalá
212 and follows the ethical guidelines of the Declaration of Helsinki (2013). Since it used
213 publicly available tweets, no human subjects or interventions were involved. However,
214 we ensured user anonymity by not disclosing names or including tweets that could reveal
215 identities.

216 **RESULTS**

217 **Total count of tweets**

218 A total of 1,570,321 tweets mentioning antidepressants in both Spanish and English were
219 collected from 2007 to 2022. Of these, 1,048,576 were in English and 521,745 in Spanish.
220 After excluding 35,448 English and 86,199 Spanish tweets that either did not meet the
221 inclusion criteria or were unintelligible, a final dataset of 1,448,674 tweets was analyzed:
222 1,013,128 in English and 435,546 in Spanish.

223 SSRIs emerged as the most frequently mentioned class of antidepressants in both
224 languages. In English tweets (Supplementary Material - Figure 1) SSRIs accounted for
225 27.9% of all mentions, while in Spanish tweets (Supplementary Material – Figure 2), they
226 constituted a significantly higher proportion at 58.91%. Variations were observed in the
227 mentions of SNRIs, TCAs, and other classes of antidepressants between the two
228 languages. In English tweets, SNRIs represented 25.71%, TCAs 11.28%, and other
229 antidepressants 19.5%. In contrast, Spanish tweets showed lower proportions for SNRIs
230 (5.72%), TCAs (4.74%), and other antidepressants (5.39%). Glutamatergic
231 antidepressants were mentioned more frequently in Spanish tweets, representing 25.24%
232 of all mentions, compared to 15.61% in English tweets.

233 **Number of tweets per year**

234 In English-language tweets, mentions of antidepressants remained stable between 2007
235 and 2020, followed by a significant increase in references to SSRIs from 2021 onwards
236 (Figure 1). A similar upward trend was observed for glutamatergic drugs starting in 2021.
237 Notably, prior to the rise in SSRI mentions, dual agents accounted for the highest volume
238 of tweets.

239 In contrast, Spanish-language tweets primarily focused on SSRIs, with notable peaks in
240 2012 and 2021. Between 2013 and 2016, there was a marked decline in SSRI mentions,
241 followed by a resurgence in 2021. Tweets referencing glutamatergic drugs showed a
242 steady increase beginning in 2011, peaking in 2017, and experiencing exponential growth
243 between 2018 and 2021 (Figure 2).

244 **Topic modeling analysis of SSRIs and glutamatergic antidepressants**

245 Following a topic modeling analysis, the most frequent themes were classified based on
246 the number of tweets and the corresponding pharmacological group. In English, the

247 themes related to SSRIs were availability and pricing (63.55% of tweets), personal
248 experiences (21.02%) and lastly tweets related to depression treatment and suicide
249 prevention (15.43%) (Figure 3). In Spanish, the themes with the highest number of tweets
250 were availability (41.6%), efficacy in depression treatment (31.7%), effects on sexuality
251 (19.14%), and lastly personal experiences (7.56%) (Figure 4).

252 Similarly, the most frequent themes in tweets discussing glutamatergic drugs were
253 classified. In English, the most frequent themes were efficacy of esketamine in TRD
254 (69.31%) and considerations regarding ketamine use (30.69%) (Figure 5). In Spanish,
255 themes included efficacy of glutamatergic drugs in TRD treatment (57.3%),
256 considerations regarding esketamine (27.7%), and recreational use of ketamine and
257 esketamine (15%) (Figure 6).

258 **Temporal analysis of the main topics related to SSRIs and glutamatergic drugs**

259 We analyzed the evolution of different topics related to SSRIs and glutamatergic drugs in
260 both English and Spanish tweets. In English, the three primary themes remained relatively
261 stable over time, with a slight increase in tweets discussing depression treatment and
262 suicide prevention noted in 2011 (Figure 7). From 2020 onwards, there was a significant
263 rise in tweets related to availability and pricing (Figure 5a). Similarly, starting in 2021,
264 there was a notable surge in tweets about glutamatergic drugs, particularly the efficacy of
265 esketamine for treatment-resistant depression (Figure 8).

266 In contrast, Spanish tweets showed greater fluctuations and thematic diversity over the
267 years. An increase in tweets about availability was observed in 2013, remaining steady
268 until another peak in 2022. Discussions on the effects of SSRIs on sexuality grew
269 gradually from 2010, with a more pronounced increase in 2022. Similarly, tweets about
270 the efficacy of SSRIs in treating depression showed a steady rise from 2010, peaking

271 again in 2022 (Figure 7). Tweets about the efficacy of glutamatergic drugs in treatment-
272 resistant depression also steadily increased, with a marked rise in discussions about
273 esketamine starting in 2021 (Figure 8).

274 **Sentiment analysis for each topic**

275 Figure 9A shows that in English tweets about SSRIs, availability and pricing elicit
276 sadness, fear, and surprise, while personal experiences are dominated by fear, and sadness
277 prevails in discussions of depression treatment and suicide prevention. In Spanish tweets
278 (Figure 9B), anger dominates conversations about availability and efficacy, while joy is
279 more prominent in discussions on sexuality and personal experiences.

280 For glutamatergic treatments in English (Figure 10A), fear and sadness are the main
281 emotions in tweets about ketamine, while esketamine's efficacy in treatment-resistant
282 depression evokes surprise, sadness, and some joy. In Spanish, anger is the predominant
283 emotion in tweets about esketamine's efficacy in treatment-resistant depression and its
284 recreational use, followed by surprise and joy in both cases (Figure 10B).

285 **DISCUSSION**

286 In this study, we analyzed over a million English and Spanish tweets posted between 2007
287 and 2022 to investigate public perceptions of antidepressants, focusing on SSRIs and
288 glutamatergic modulators. Using artificial intelligence techniques such as sentiment
289 analysis and topic modeling, we identified key concerns, emotions, and cultural
290 differences in the discussions surrounding these medications. Our findings reveal that
291 SSRIs were the most frequently mentioned antidepressants in both languages, with
292 pricing and availability being key concerns, particularly in English tweets, while Spanish
293 tweets often emphasized efficacy and sexual side effects. Additionally, discussions
294 around esketamine for treatment-resistant depression gained traction in recent years, with

295 notable differences in emotional responses between languages. These findings provide
296 real-time insights into public attitudes, highlighting the influence of social and cultural
297 contexts on the perception and acceptance of antidepressants, especially in light of the
298 growing global focus on mental health.

299 SSRIs are the most widely used antidepressants globally, recommended as first-line
300 treatment for depressive disorders [11,12,62] and a range of psychiatric conditions [63].
301 This broad use likely explains their prominence in both English and Spanish tweets, a
302 trend seen in previous studies [52]. Notably, in Spanish tweets, we observed two distinct
303 peaks: one in 2013 and another, in 2022. The 2013 increase aligns with national reports
304 from Spain, which documented a 200% rise in antidepressant use between 2000 and 2013,
305 with SSRIs showing a 159.3% increase [64] likely tied to the economic crisis and the
306 arise of mental health issues during this period. Both language groups showed a
307 significant rise in SSRI-related tweets between 2020 and 2022, coinciding with the
308 COVID-19 pandemic, which drove a global rise in SSRIs antidepressant prescriptions
309 [65,66], particularly among adolescents and young adults [67].

310 Our analysis of tweets discussing SSRIs revealed that drug availability was a key concern
311 in both languages, with anger dominating Spanish tweets and sadness, fear, and surprise
312 being more common in English tweets. These emotions reflect real-world challenges like
313 shortages and price increases during the pandemic, especially in countries like the UK
314 and the US [68,69]. Similar concerns have been reported in Latin American countries,
315 where shortages of medications, particularly antidepressants, have raised alarm [70].

316 In English tweets, the availability and pricing of SSRIs were also major topics of
317 discussion on X, particularly in 2021 and 2022. By 2020, the cost of prescribing SSRIs
318 in countries like the UK had tripled compared to 2019, largely due to shortages of active
319 pharmaceutical ingredients and the increased cost of generic drugs during the pandemic

320 [71]. Similarly, the United States saw drug costs rise, with Medicaid expenditures on
321 antidepressants increasing from \$1 billion in 2017 to \$1.12 billion in 2021, with SSRIs
322 accounting for the largest share [72,73]. In contrast, the lower focus on pricing in Spanish
323 tweets might reflect differences in healthcare systems, such as the broader coverage
324 provided by Spain's public healthcare system. These findings highlight how X mirrors
325 key societal issues, but further research is needed to fully understand the interplay
326 between language, region, and healthcare context in shaping these discussions. Previous
327 studies have proposed using social media information as a pharmacovigilance tool due to
328 its immediacy and timeliness [69].

329 The efficacy and use of SSRIs were frequently discussed in both languages, but with
330 notable emotional differences. Spanish tweets often expressed anger, along with some joy
331 and sadness. The prominent anger may be attributed to the delay in SSRIs' therapeutic
332 effects, as these medications typically take several weeks to become effective [74]. This
333 delay can lead to frustration or anger among patients seeking immediate relief.

334 Previous research by Leis et al. [75] found that patients undergoing SSRI treatment
335 showed small but statistically significant increases in happiness and surprise emotions,
336 without significant changes in sadness, anger, fear, or disgust. This contrast with the lower
337 levels of joy observed in our study, emphasizing the nuanced emotional responses
338 associated with SSRI treatment. Interestingly, Leis et al. also reported a slight increase in
339 the use of negations during the treatment period, potentially reflecting ongoing concerns
340 or dissatisfaction. Further research is needed to better understand the underlying reasons
341 for these emotional reactions, as this knowledge could provide valuable insights for
342 clinicians when managing patient expectations and experiences with these medications.

343 In contrast, English tweets focused more on the role of SSRIs in suicide prevention, a
344 topic that remains controversial. Many English tweets expressed fear and sadness,

345 reflecting ongoing public concern about the potential link between SSRIs and increased
346 suicidal ideation, particularly in adolescents and young adults. Since 2004, regulatory
347 agencies have issued warnings about this risk in younger populations [76], and although
348 meta-analyses since 2009 have examined the relationship between antidepressants and
349 suicidal thoughts [11], the evidence remains inconclusive [77]. While some studies
350 suggest efficacy in treating depression but an increased risk of suicidal acts in young
351 people, others show no increased risk in adults, with some even indicating protective
352 effects against suicide in adults [77–82].

353 The emotional tone in these discussions highlights the complexity of the issue, and the
354 need for further research. Social media platforms like X could play a vital role in detecting
355 depressive symptoms and suicidal behaviors [83,84], particularly among vulnerable
356 groups like adolescents, making this an important area for future research.

357 Many drugs, such as antidepressants, can cause adverse effects if abruptly discontinued
358 [85], making early detection of drug shortages through social media potentially beneficial
359 for both patients and healthcare professionals. A prominent theme in Spanish tweets, not
360 present in English tweets, was the impact of SSRIs on sexual function, with emotions
361 primarily reflecting joy, surprise, and anger. While the anger may be related to the well-
362 documented sexual side effects of SSRIs, such as reduced libido and sexual dysfunction
363 [86–89], these associations should be interpreted with caution, as they cannot be
364 definitively established based solely on social media data. Similarly, the expressions of
365 joy and surprise could be linked to the use of SSRIs for premature ejaculation, where they
366 are often prescribed due to their safety, tolerability, and efficacy [90,91].

367 Emotional tones in tweets are influenced by a variety of factors, including individual
368 experiences, cultural attitudes toward discussing sexuality, and the healthcare context in
369 different Spanish-speaking regions. The higher volume of discussions about sexual

370 effects in Spanish tweets suggests strong public interest in this topic, highlighting the
371 importance of providing patients with clear information about these potential side effects
372 before initiating treatment.

373 Since 2019, there has been a significant increase in tweets mentioning glutamatergic
374 drugs, especially esketamine, in both English and Spanish. This surge aligns with the FDA
375 and EMA approval of esketamine for TRD in 2019 [92], indicating that discussions on X
376 reflect ongoing clinical developments. Esketamine, notable for its novel mechanism
377 targeting NMDA receptors and its intranasal administration, has gained attention as a
378 promising option in TRD and other psychiatric conditions, [93,94]. Our analysis shows
379 that both English and Spanish tweets primarily focused on the efficacy of esketamine in
380 TRD, though Spanish tweets also emphasized glutamatergic modulators in general. While
381 short-term efficacy is well-supported by evidence [95,96], uncertainty remains regarding
382 long-term outcomes, with mixed research findings on sustained benefits [97–99].
383 Esketamine is better than placebo in the relapse rate and the remission rate at 32 weeks
384 of follow up [97] and although it is approved in the majority of European countries, it has
385 not been approved in the United Kingdom by the Nice guidelines [99]. These doubts also
386 extend to ketamine, influencing public perceptions and emotional responses on social
387 media.

388 A recent study by Ng et al. [100] found a shift in public attitudes after esketamine's
389 approval, with discussions centered on regulatory changes, cautious optimism, and
390 positive personal experiences, which partially align with our findings. Sentiment analysis
391 revealed that, in English tweets, emotions like surprise and sadness dominated, though
392 joy was also present, reflecting hope and optimism regarding esketamine and ketamine
393 treatments. In contrast, Spanish tweets showed more anger, likely due to skepticism or

394 frustration over high costs and limited access, but joy was also evident, indicating that
395 these treatments still inspire hope among Spanish-speaking users.

396 Interestingly, we found that recreational use of ketamine and esketamine was the third
397 most commented topic in Spanish tweets, but not in English ones. Recreational ketamine
398 use has risen in recent years, with a significant increase in ketamine seizures in the United
399 States between 2017 and 2022 [101]. Spain has also seen a rise in use, with 0.9% of the
400 population reporting ketamine use at least once between 2020 and 2022 [102]. South
401 America has reported emerging trends of ketamine use, including its combination with
402 other substances, such as in the new concoction "Tusi" (composed of ketamine and often
403 combined with substances like MDMA, methamphetamine, cocaine, opioids, and new
404 psychoactive substances), which has gained popularity in multiple regions [103].

405 The increase in recreational use is reflected in social media discussions, where our
406 sentiment analysis found anger to be the predominant emotion, followed by surprise and
407 joy. Anger may stem from concerns about the trivialisation of ketamine's therapeutic uses,
408 as has occurred with other medications that have also become recreational drugs
409 [104,105]. However, a 2022 study by Grabski et al. [106] found no significant changes
410 in public perceptions of ketamine's risks following the approval of esketamine for
411 medical use. They highlight the importance of clearly communicating the risks of
412 recreational ketamine use in discussions about its therapeutic benefits. Further research
413 into these recreational uses on social media platforms like X is warranted.

414 This study relied solely on Twitter data, which may not represent the broader patient
415 population, as Twitter users tend to be younger and more tech-savvy. To strengthen the
416 analysis, other social media platforms or traditional research should be considered.
417 Tweets' character limits can lead to incomplete or unclear messages, often missing key
418 context about the user's condition or treatment. Variations in drug names and misspellings

419 can also distort sentiment. Additionally, since only Spanish and English tweets were
420 analysed, the findings may not apply globally.

421 Cultural attitudes influence the emotional responses seen in this study, highlighting the
422 need to consider context when evaluating public perceptions of psychiatric treatments as
423 antidepressants. Differences between regions sharing the same language may further
424 shape these perceptions, reflecting variations in healthcare systems, social norms, and
425 access to treatments.

426 Our results emphasise the importance of further research and spreading accurate
427 information on social media to improve perceptions and reduce misunderstandings. On
428 X, antidepressants, especially SSRIs, are discussed with optimism and concerns about
429 availability, pricing, personal experiences, and efficacy, shaped by cultural differences.
430 Glutamatergic modulators, like ketamine and esketamine, have drawn attention for TRD,
431 with Spanish tweets noting concerns about recreational use. This study shows social
432 media's potential to complement traditional research, though its limitations call for
433 cautious interpretation and more research to improve its role in pharmacovigilance and
434 public health.

435 **Conflicts of Interest Statement**

436 Dr Salazar-de-Pablo has received honoraria from Janssen Cilag, Lundbeck, Angelini and
437 Menarini. Dr. Gonzalez-Pinto has received grants and served as consultant, advisor or
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457 **Data availability**

458 The datasets generated and analyzed during the current study are available from the
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460 collection and variables analyzed can be found in the supplementary material provided
461 with this manuscript.

462 **Supplementary Material**

463 For Supplementary Material accompanying this paper, visit cambridge.org/EPA.

464 **Figure Legends**

465 Figure 1: Number of tweets in English per year per drug. Each antidepressant group has
466 its own color represented in left superior corner of the panel.

467 Figure 2: Number of tweets in Spanish per year per drug. Each antidepressant group has
468 its own color represented in left superior corner of the panel.

469 Figure 3: Number of tweets per topic in SSRI in English. Each topic has its own color
470 represented in left superior corner of the panel.

471 Figure 4: Number of tweets per topic in SSRI in Spanish. Each topic has its own color
472 represented in left superior corner of the panel.

473 Figure 5: Number of tweets per topic in glutamatergic drugs in English. Each topic has
474 its own color represented in left superior corner of the panel.

475 Figure 6: Number of tweets per topic in glutamatergic drugs in Spanish. Each topic has
476 its own color represented in right superior corner of the panel.

477 Figure 7: Temporal evolution of the number of tweets related to SSRIs, per year and topic,
478 in English (superior panel) and Spanish (bottom panel).

479 Figure 8: Temporal evolution of the number of tweets related to glutamatergic drugs, per
480 year and topic, in English (superior panel) and Spanish (bottom panel).

481 Figure 9: Sentiment analysis of the number of tweets per year and topic in English (A)
482 and Spanish (B) tweets from SSRIs.

483 Figure 10: Sentiment analysis of the number of tweets per year and topic in English (A)
484 and Spanish (B) tweets from glutamatergic drugs.

485 **References**

- 486 1. Brauer, R.; Alfageh, B.; Blais, J.E.; Chan, E.W.; Chui, C.S.L.; Hayes, J.F.; Man,
487 K.K.C.; Lau, W.C.Y.; Yan, V.K.C.; Beykloo, M.Y.; et al. Psychotropic Medicine
488 Consumption in 65 Countries and Regions, 2008–19: A Longitudinal Study.
489 *Lancet Psychiatry* **2021**, *8*, 1071–1082, doi:10.1016/S2215-0366(21)00292-3.
- 490 2. Global Burden of 369 Diseases and Injuries in 204 Countries and Territories,
491 1990-2019: A Systematic Analysis for the Global Burden of Disease Study 2019.
492 *Lancet* **2020**, *396*, 1204–1222, doi:10.1016/S0140-6736(20)30925-9.
- 493 3. Santomauro, D.F.; Mantilla Herrera, A.M.; Shadid, J.; Zheng, P.; Ashbaugh, C.;
494 Pigott, D.M.; Abbafati, C.; Adolph, C.; Amlag, J.O.; Aravkin, A.Y.; et al. Global
495 Prevalence and Burden of Depressive and Anxiety Disorders in 204 Countries
496 and Territories in 2020 Due to the COVID-19 Pandemic. *The Lancet* **2021**, *398*,
497 1700–1712, doi:10.1016/S0140-6736(21)02143-7.
- 498 4. Whiteford, H.A.; Degenhardt, L.; Rehm, J.; Baxter, A.J.; Ferrari, A.J.; Erskine,
499 H.E.; Charlson, F.J.; Norman, R.E.; Flaxman, A.D.; Johns, N.; et al. Global
500 Burden of Disease Attributable to Mental and Substance Use Disorders:
501 Findings from the Global Burden of Disease Study 2010. *The Lancet* **2013**, *382*,
502 1575–1586, doi:10.1016/S0140-6736(13)61611-6.
- 503 5. American Psychiatric Association - *Diagnostic and Statistical Manual of Mental*
504 *Disorders (DSM-5®)*; Arlington, TX, USA, 2013;
- 505 6. González-Ortega, I.; Diaz-Marsa, M.; López-Peña, P.; Fernández-Sevillano, J.;
506 Andreo-Jover, J.; Bobes, J.; Bravo-Ortiz, M.F.; Cebria, A.I.; Crespo-Facorro, B.;
507 de la Torre-Luque, A.; et al. Clinical Predictors and Psychosocial Risk Factors of
508 Suicide Attempt Severity. *Spanish Journal of Psychiatry and Mental Health* **2023**,
509 doi:10.1016/J.SJPMH.2023.07.002.
- 510 7. Fusar-Poli, P. Integrated Mental Health Services for the Developmental Period (0
511 to 25 Years): A Critical Review of the Evidence. *Front Psychiatry* **2019**, *10*, 355,
512 doi:10.3389/FPSYT.2019.00355.
- 513 8. Lépine, J.P.; Briley, M. The Increasing Burden of Depression. *Neuropsychiatr Dis*
514 *Treat* **2011**, *7*, 3–7, doi:10.2147/NDT.S19617.
- 515 9. Cipriani, A.; Furukawa, T.A.; Salanti, G.; Chaimani, A.; Atkinson, L.Z.; Ogawa, Y.;
516 Leucht, S.; Ruhe, H.G.; Turner, E.H.; Higgins, J.P.T.; et al. Comparative Efficacy
517 and Acceptability of 21 Antidepressant Drugs for the Acute Treatment of Adults
518 with Major Depressive Disorder: A Systematic Review and Network Meta-
519 Analysis. *Lancet* **2018**, *391*, 1357–1366, doi:10.1016/S0140-6736(17)32802-7.
- 520 10. Kishi, T.; Ikuta, T.; Sakuma, K.; Okuya, M.; Hatano, M.; Matsuda, Y.; Iwata, N.
521 Antidepressants for the Treatment of Adults with Major Depressive Disorder in
522 the Maintenance Phase: A Systematic Review and Network Meta-Analysis.
523 *Molecular Psychiatry* **2022**, *28*, 402–409, doi:10.1038/s41380-022-
524 01824-z.
- 525 11. Overview | Depression in Adults: Treatment and Management | Guidance |
526 NICE.

- 527 12. Patten, S.B. Updated CANMAT Guidelines for Treatment of Major Depressive
528 Disorder. <http://dx.doi.org/10.1177/0706743716660034> **2016**, *61*, 504–505,
529 doi:10.1177/0706743716660034.
- 530 13. Mercier, A.; Auger-Aubin, I.; Lebeau, J.P.; Schuers, M.; Boulet, P.; Hermil, J.L.;
531 Van Royen, P.; Peremans, L. Evidence of Prescription of Antidepressants for
532 Non-Psychiatric Conditions in Primary Care: An Analysis of Guidelines and
533 Systematic Reviews. *BMC Fam Pract* **2013**, *14*, 55, doi:10.1186/1471-2296-14-
534 55.
- 535 14. Schatzberg, A.F. New Indications for Antidepressants. *J Clin Psychiatry* **2000**,
536 *61*, 9008.
- 537 15. Sheffler, Z.M.; Patel, P.; Abdijadid, S. Antidepressants. *StatPearls* **2023**.
- 538 16. Gill, H.; Gill, B.; El-Halabi, S.; Chen-Li, D.; Lipsitz, O.; Rosenblat, J.D.; Van
539 Rheenen, T.E.; Rodrigues, N.B.; Mansur, R.B.; Majeed, A.; et al. Antidepressant
540 Medications and Weight Change: A Narrative Review. *Obesity* **2020**, *28*, 2064–
541 2072, doi:10.1002/OBY.22969.
- 542 17. Short, B.; Fong, J.; Galvez, V.; Shelker, W.; Loo, C.K. Side-Effects Associated
543 with Ketamine Use in Depression: A Systematic Review. *Lancet Psychiatry* **2018**,
544 *5*, 65–78, doi:10.1016/S2215-0366(17)30272-9.
- 545 18. Zhou, X.; Teng, T.; Zhang, Y.; Del Giovane, C.; Furukawa, T.A.; Weisz, J.R.; Li,
546 X.; Cuijpers, P.; Coghill, D.; Xiang, Y.; et al. Comparative Efficacy and
547 Acceptability of Antidepressants, Psychotherapies, and Their Combination for
548 Acute Treatment of Children and Adolescents with Depressive Disorder: A
549 Systematic Review and Network Meta-Analysis. *Lancet Psychiatry* **2020**, *7*, 581–
550 601, doi:10.1016/S2215-0366(20)30137-1.
- 551 19. Moncrieff, J.; Wessely, S.; Hardy, R. Active Placebos versus Antidepressants for
552 Depression. *Cochrane Database Syst Rev* **2004**, *2004*,
553 doi:10.1002/14651858.CD003012.PUB2.
- 554 20. Pigott, H.E.; Leventhal, A.M.; Alter, G.S.; Boren, J.J. Efficacy and Effectiveness
555 of Antidepressants: Current Status of Research. *Psychother Psychosom* **2010**,
556 *79*, 267–279, doi:10.1159/000318293.
- 557 21. Khan, A.; Brown, W.A. Antidepressants versus Placebo in Major Depression: An
558 Overview. *World Psychiatry* **2015**, *14*, 294–300, doi:10.1002/WPS.20241.
- 559 22. Serretti, A.; Chiesa, A. Treatment-Emergent Sexual Dysfunction Related to
560 Antidepressants: A Meta-Analysis. *J Clin Psychopharmacol* **2009**, *29*, 259–266,
561 doi:10.1097/JCP.0B013E3181A5233F.
- 562 23. Montgomery, S.A.; Baldwin, D.S.; Riley, A. Antidepressant Medications: A
563 Review of the Evidence for Drug-Induced Sexual Dysfunction. *J Affect Disord*
564 **2002**, *69*, 119–140, doi:10.1016/S0165-0327(01)00313-5.
- 565 24. McIntyre, R.S.; Alsuwaidan, M.; Baune, B.T.; Berk, M.; Demyttenaere, K.;
566 Goldberg, J.F.; Gorwood, P.; Ho, R.; Kasper, S.; Kennedy, S.H.; et al. Treatment-
567 resistant Depression: Definition, Prevalence, Detection, Management, and
568 Investigational Interventions. *World Psychiatry* **2023**, *22*, 394,
569 doi:10.1002/WPS.21120.

- 570 25. McAllister-Williams, R.H.; Arango, C.; Blier, P.; Demyttenaere, K.; Falkai, P.;
571 Gorwood, P.; Hopwood, M.; Javed, A.; Kasper, S.; Malhi, G.S.; et al. The
572 Identification, Assessment and Management of Difficult-to-Treat Depression: An
573 International Consensus Statement. *J Affect Disord* **2020**, *267*, 264–282,
574 doi:10.1016/J.JAD.2020.02.023.
- 575 26. McAllister-Williams, R.H.; Arango, C.; Blier, P.; Demyttenaere, K.; Falkai, P.;
576 Gorwood, P.; Hopwood, M.; Javed, A.; Kasper, S.; Malhi, G.S.; et al. The
577 Identification, Assessment and Management of Difficult-to-Treat Depression: An
578 International Consensus Statement. *J Affect Disord* **2020**, *267*, 264–282,
579 doi:10.1016/J.JAD.2020.02.023.
- 580 27. Gaynes, B.N.; Lux, L.; Gartlehner, G.; Asher, G.; Forman-Hoffman, V.; Green, J.;
581 Boland, E.; Weber, R.P.; Randolph, C.; Bann, C.; et al. Defining Treatment-
582 Resistant Depression. *Depress Anxiety* **2020**, *37*, 134–145,
583 doi:10.1002/DA.22968.
- 584 28. Salazar De Pablo, G.; Studerus, E.; Vaquerizo-Serrano, J.; Irving, J.; Catalan, A.;
585 Oliver, D.; Baldwin, H.; Danese, A.; Fazel, S.; Steyerberg, E.W.; et al.
586 Implementing Precision Psychiatry: A Systematic Review of Individualized
587 Prediction Models for Clinical Practice. *Schizophr Bull* **2021**, *47*, 284–297,
588 doi:10.1093/SCHBUL/SBAA120.
- 589 29. Jacob, S.A.; Ab Rahman, A.F.; Ahmad Hassali, M.A. Attitudes and Beliefs of
590 Patients with Chronic Depression toward Antidepressants and Depression.
591 *Neuropsychiatr Dis Treat* **2015**, *11*, 1339, doi:10.2147/NDT.S82563.
- 592 30. Chakraborty, K.; Avasthi, A.; Kumar, S.; Grover, S. Attitudes and Beliefs of
593 Patients of First Episode Depression towards Antidepressants and Their
594 Adherence to Treatment. *Soc Psychiatry Psychiatr Epidemiol* **2009**, *44*, 482–
595 488, doi:10.1007/S00127-008-0468-0.
- 596 31. Corcoran, T.B.; Haigh, F.; Seabrook, A.; Schug, S.A. A Survey of Patients' Use of
597 the Internet for Chronic Pain-Related Information. *Pain Med* **2010**, *11*, 512–517,
598 doi:10.1111/J.1526-4637.2010.00817.X.
- 599 32. Haslam, C.; Brown, S.; Atkinson, S.; Haslam, R. Patients' Experiences of
600 Medication for Anxiety and Depression: Effects on Working Life. *Fam Pract*
601 **2004**, *21*, 204–212, doi:10.1093/FAMPRA/CMH218.
- 602 33. Hidalgo-Mazzei, D.; Mantingh, T.; Pérez de Mendiola, X.; Samalin, L.;
603 Undurraga, J.; Strojilovich, S.; Severus, E.; Bauer, M.; González-Pinto, A.;
604 Nolen, W.A.; et al. Clinicians' Preferences and Attitudes towards the Use of
605 Lithium in the Maintenance Treatment of Bipolar Disorders around the World: A
606 Survey from the ISBD Lithium Task Force. *Int J Bipolar Disord* **2023**, *11*, 20,
607 doi:10.1186/S40345-023-00301-Y.
- 608 34. Windschitl, P.D.; Miller, J.E.; Park, I.; Rule, S.; Clary, A.; Smith, A.R. The
609 Desirability Bias in Predictions under Aleatory and Epistemic Uncertainty.
610 *Cognition* **2022**, *229*, doi:10.1016/J.COGNITION.2022.105254.
- 611 35. Farrar, M.; Lundt, L.; Franey, E.; Yonan, C. Patient Perspective of Tardive
612 Dyskinesia: Results from a Social Media Listening Study. *BMC Psychiatry* **2021**,
613 *21*, doi:10.1186/S12888-021-03074-9.

- 614 36. Leonardo, N.; Lester, S.; Graham, M.; Barrett, C.; Whittle, S.; Rowett, D.;
615 Buchbinder, R.; Hill, C.L. Selection and Perception of Methotrexate Treatment
616 Information in People with Rheumatoid Arthritis. *Int J Rheum Dis* **2020**, *23*, 805–
617 812, doi:10.1111/1756-185X.13833.
- 618 37. Robinson, P.; Turk, D.; Jilka, S.; Cella, M. Measuring Attitudes towards Mental
619 Health Using Social Media: Investigating Stigma and Trivialisation. *Soc*
620 *Psychiatry Psychiatr Epidemiol* **2019**, *54*, 51–58, doi:10.1007/S00127-018-1571-
621 5.
- 622 38. Farsi, D.; Martinez-Menchaca, H.R.; Ahmed, M.; Farsi, N. Social Media and
623 Health Care (Part II): Narrative Review of Social Media Use by Patients. *J Med*
624 *Internet Res* **2022**, *24*, e30379, doi:10.2196/30379.
- 625 39. Khademi, S.; Hallinan, C.M.; Conway, M.; Bonomo, Y. Using Social Media Data
626 to Investigate Public Perceptions of Cannabis as a Medicine: Narrative Review. *J*
627 *Med Internet Res* **2023**, *25*, doi:10.2196/36667.
- 628 40. Moorhead, S.A.; Hazlett, D.E.; Harrison, L.; Carroll, J.K.; Irwin, A.; Hoving, C. A
629 New Dimension of Health Care: Systematic Review of the Uses, Benefits, and
630 Limitations of Social Media for Health Communication. *J Med Internet Res* **2013**,
631 *15*, 6, doi:10.2196/JMIR.1933.
- 632 41. Alvarez-Mon, M.A.; Donat-Vargas, C.; Santoma-Vilaclara, J.; Anta, L. de; Goena,
633 J.; Sanchez-Bayona, R.; Mora, F.; Ortega, M.A.; Lahera, G.; Rodriguez-Jimenez,
634 R.; et al. Assessment of Antipsychotic Medications on Social Media: Machine
635 Learning Study. *Front Psychiatry* **2021**, *12*, doi:10.3389/FPSYT.2021.737684.
- 636 42. R. Scott, K.; Nelson, L.; Meisel, Z.; Perrone, J. Opportunities for Exploring and
637 Reducing Prescription Drug Abuse Through Social Media. *J Addict Dis* **2015**, *34*,
638 178–184, doi:10.1080/10550887.2015.1059712.
- 639 43. Choo, E.K.; Mazer-Amirshahi, M.; Juurlink, D.; Kobner, S.; Scott, K.; Lin, M. The
640 Prescription Opioid Epidemic: Social Media Responses to the Residents'
641 Perspective Article. *Ann Emerg Med* **2016**, *67*, 40–48,
642 doi:10.1016/J.ANNEMERGEMED.2015.05.005.
- 643 44. Chen, X.; Faviez, C.; Schuck, S.; Lillo-Le-Louët, A.; Texier, N.; Dahamna, B.;
644 Huot, C.; Foulquié, P.; Pereira, S.; Leroux, V.; et al. Mining Patients' Narratives in
645 Social Media for Pharmacovigilance: Adverse Effects and Misuse of
646 Methylphenidate. *Front Pharmacol* **2018**, *9*, 541,
647 doi:10.3389/FPHAR.2018.00541.
- 648 45. Golder, S.; Norman, G.; Loke, Y.K. Systematic Review on the Prevalence,
649 Frequency and Comparative Value of Adverse Events Data in Social Media. *Br J*
650 *Clin Pharmacol* **2015**, *80*, 878–888, doi:10.1111/BCP.12746.
- 651 46. van Stekelenborg, J.; Ellenius, J.; Maskell, S.; Bergvall, T.; Caster, O.; Dasgupta,
652 N.; Dietrich, J.; Gama, S.; Lewis, D.; Newbould, V.; et al. Recommendations for
653 the Use of Social Media in Pharmacovigilance: Lessons from IMI WEB-RADR.
654 *Drug Saf* **2019**, *42*, 1393–1407, doi:10.1007/S40264-019-00858-7.
- 655 47. Pappa, D.; Stergioulas, L.K. Harnessing Social Media Data for
656 Pharmacovigilance: A Review of Current State of the Art, Challenges and Future

- 657 Directions. *Int J Data Sci Anal* **2019**, *8*, 113–135, doi:10.1007/S41060-019-
658 00175-3/TABLES/4.
- 659 48. Choudhury, M. De; Gamon, M.; ... S.C.-P. of the; 2013, undefined Predicting
660 Depression via Social Media. *ojs.aaai.org* M De Choudhury, M Gamon, S Counts,
661 E Horvitz Proceedings of the international AAAI conference on web and social
662 media, 2013•ojs.aaai.org **2013**.
- 663 49. Leis, A.; Ronzano, F.; Mayer, M.A.; Furlong, L.I.; Sanz, F. Detecting Signs of
664 Depression in Tweets in Spanish: Behavioral and Linguistic Analysis. *J Med*
665 *Internet Res* **2019**, *21*, doi:10.2196/14199.
- 666 50. de Anta, L.; Alvarez-Mon, M.A.; Ortega, M.A.; Salazar, C.; Donat-Vargas, C.;
667 Santoma-Vilaclara, J.; Martin-Martinez, M.; Lahera, G.; Gutierrez-Rojas, L.;
668 Rodriguez-Jimenez, R.; et al. Areas of Interest and Social Consideration of
669 Antidepressants on English Tweets: A Natural Language Processing
670 Classification Study. *J Pers Med* **2022**, *12*, doi:10.3390/JPM12020155.
- 671 51. de las Cuevas, C.; Gutiérrez-Rojas, L.; Alvarez-Mon, M.A.; Andreu-Bernabeu, Á.;
672 Capitán, L.; Gómez, J.C.; Grande, I.; Hidalgo-Mazzei, D.; Mateos, R.; Moreno-
673 Gea, P.; et al. Evaluating the Effect of a Telepsychiatry Educational Program on
674 the Awareness, Knowledge, Attitude, and Skills of Telepsychiatry Among
675 Spanish Psychiatrists during COVID-19 Pandemic. *Telemed J E Health* **2023**,
676 *29*, doi:10.1089/TMJ.2022.0051.
- 677 52. Dong, Y.; Weir, N.M. Antidepressants: A Content Analysis of Healthcare
678 Providers' Tweets. *Exploratory research in clinical and social pharmacy* **2023**, *9*,
679 doi:10.1016/J.RCSOP.2023.100232.
- 680 53. Kulli, N.; Senbel, S. COVID-19 Vaccine Response on Social Media Using LDA
681 Analysis. *Lecture Notes in Networks and Systems* **2024**, *920 LNNS*, 70–77,
682 doi:10.1007/978-3-031-53963-3_7.
- 683 54. Ramamoorthy, T.; Kulothungan, V.; Mappillairaju, B. Topic Modeling and Social
684 Network Analysis Approach to Explore Diabetes Discourse on Twitter in India.
685 *Front Artif Intell* **2024**, *7*, 1329185, doi:10.3389/FRAI.2024.1329185/BIBTEX.
- 686 55. Di Vincenzo, D.; Greselin, F.; Piacenza, F.; Zitakis, R. A Text Analysis for
687 Operational Risk Loss Descriptions. *SSRN Electronic Journal* **2023**,
688 doi:10.2139/SSRN.4286208.
- 689 56. Arbelaitz, O.; Gurrutxaga, I.; Muguerza, J.; Pérez, J.M.; Perona, I. An Extensive
690 Comparative Study of Cluster Validity Indices. *Pattern Recognit* **2013**, *46*, 243–
691 256, doi:10.1016/J.PATCOG.2012.07.021.
- 692 57. Domingo-Espiñeira, J.; Information, O.F.-M.-; 2024, undefined Navigating the
693 Digital Neurolandscape: Analyzing the Social Perception of and Sentiments
694 Regarding Neurological Disorders through Topic Modeling And. *mdpi.com* J
695 Domingo-Espiñeira, O Fraile-Martínez, C Garcia-Montero, M Montero, A
696 Varaona Information, 2024•mdpi.com.
- 697 58. Valades, M.T.; Montero-Torres, M.; Lara-Abelenda, F.J.; Carabot, F.; Ortega,
698 M.A.; Álvarez-Mon, M.; Alvarez-Mon, M.A. Understanding Public Perceptions
699 and Discussions on Diseases Involving Chronic Pain through Social Media:

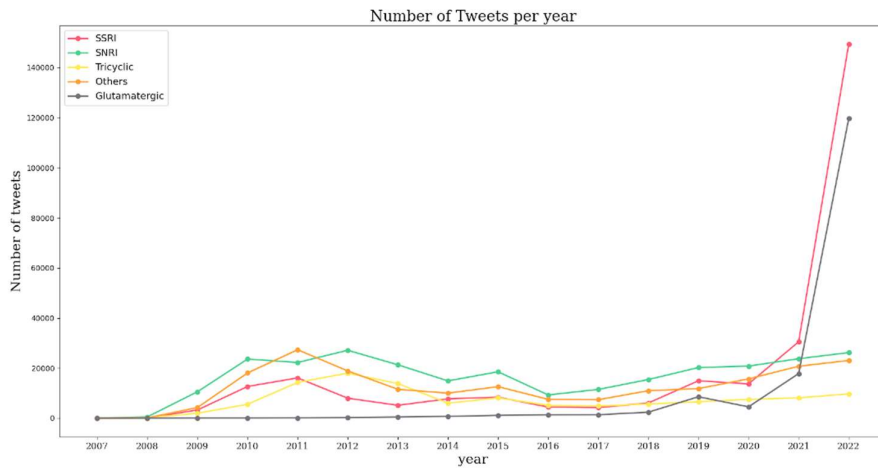
- 700 Cross-Sectional Infodemiology Study. *BMC Musculoskelet Disord* **2024**, *25*,
701 doi:10.1186/S12891-024-07687-5.
- 702 59. Hartmann, J. Emotion English DistilRoBERTa-Base Available online:
703 <https://huggingface.co/j-hartmann/emotion-english-distilroberta-base> (accessed
704 on 4 July 2023).
- 705 60. Ekman, P. Basic Emotions. *Handbook of Cognition and Emotion* **2005**, 45–60,
706 doi:10.1002/0470013494.CH3.
- 707 61. Pérez, J.M.; Furman, D.A.; Alemany, L.A.; Luque, F. RoBERTuito: A Pre-Trained
708 Language Model for Social Media Text in Spanish. *2022 Language Resources
709 and Evaluation Conference, LREC 2022* **2021**, 7235–7243.
- 710 62. Clevenger, S.S.; Malhotra, D.; Dang, J.; Vanle, B.; IsHak, W.W. The Role of
711 Selective Serotonin Reuptake Inhibitors in Preventing Relapse of Major
712 Depressive Disorder. *Ther Adv Psychopharmacol* **2018**, *8*, 49–58,
713 doi:10.1177/2045125317737264/ASSET/IMAGES/LARGE/10.1177_2045125317
714 737264-FIG1.JPEG.
- 715 63. Chu, A.; Wadhwa, R. Selective Serotonin Reuptake Inhibitors. *Veterinary
716 Psychopharmacology* **2023**, 103–128, doi:10.1002/9781119226253.ch8.
- 717 64. Agencia española de medicamentos y productos sanitarios Utilización de
718 Medicamentos Antidepresivos En España Durante El Periodo 2000-2013.
- 719 65. Kupcova, I.; Danisovic, L.; Klein, M.; Harsanyi, S. Effects of the COVID-19
720 Pandemic on Mental Health, Anxiety, and Depression. *BMC Psychol* **2023**, *11*,
721 doi:10.1186/S40359-023-01130-5.
- 722 66. Diaz-Camal, N.; Cardoso-Vera, J.D.; Islas-Flores, H.; Gómez-Oliván, L.M.;
723 Mejía-García, A. Consumption and Occurrence of Antidepressants (SSRIs) in
724 Pre- and Post-COVID-19 Pandemic, Their Environmental Impact and Innovative
725 Removal Methods: A Review. *Science of The Total Environment* **2022**, *829*,
726 154656, doi:10.1016/J.SCITOTENV.2022.154656.
- 727 67. Chua, K.P.; Volerman, A.; Zhang, J.; Hua, J.; Conti, R.M. Antidepressant
728 Dispensing to US Adolescents and Young Adults: 2016-2022. *Pediatrics* **2024**,
729 *153*, doi:10.1542/PEDS.2023-064245/196655.
- 730 68. Shukar, S.; Zahoor, F.; Hayat, K.; Saeed, A.; Gillani, A.H.; Omer, S.; Hu, S.;
731 Babar, Z.U.D.; Fang, Y.; Yang, C. Drug Shortage: Causes, Impact, and Mitigation
732 Strategies. *Front Pharmacol* **2021**, *12*, doi:10.3389/FPHAR.2021.693426.
- 733 69. Song, H.; Pei, X.; Liu, Z.; Shen, C.; Sun, J.; Liu, Y.; Zhou, L.; Sun, F.; Xiao, X.
734 Pharmacovigilance in China: Evolution and Future Challenges. *Br J Clin
735 Pharmacol* **2023**, *89*, 510–522, doi:10.1111/BCP.15277.
- 736 70. Acosta, A.; Vanegas, E.P.; Rovira, J.; Godman, B.; Bochenek, T. Medicine
737 Shortages: Gaps Between Countries and Global Perspectives. *Front Pharmacol*
738 **2019**, *10*, doi:10.3389/FPHAR.2019.00763.
- 739 71. Rabeea, S.A.; Merchant, H.A.; Khan, M.U.; Kow, C.S.; Hasan, S.S. Surging
740 Trends in Prescriptions and Costs of Antidepressants in England amid COVID-
741 19. *DARU Journal of Pharmaceutical Sciences* **2021**, *29*, 217,
742 doi:10.1007/S40199-021-00390-Z.

- 743 72. Rome, B.N.; Egilman, A.C.; Kesselheim, A.S. Trends in Prescription Drug
744 Launch Prices, 2008-2021. *JAMA* **2022**, *327*, 2145–2147,
745 doi:10.1001/JAMA.2022.5542.
- 746 73. Elmarasi, M.; Fuehrlein, B. US Medicaid Program: An Analysis of the Spending
747 and Utilization Patterns for Antidepressants from 2017 to 2021. *Exploratory*
748 *Research in Clinical and Social Pharmacy* **2024**, *13*, 100392,
749 doi:10.1016/J.RCSOP.2023.100392.
- 750 74. Kinney, G.G.; Taber, M.T.; Gribkoff, V.K. The Augmentation Hypothesis for
751 Improvement of Antidepressant Therapy: Is Pindolol a Suitable Candidate for
752 Testing the Ability of 5HT1A Receptor Antagonists to Enhance SSRI Efficacy and
753 Onset Latency? *Mol Neurobiol* **2000**, *21*, 137–152, doi:10.1385/MN:21:3:137.
- 754 75. Leis, A.; Ronzano, F.; Mayer, M.A.; Furlong, L.I.; Sanz, F. Evaluating Behavioral
755 and Linguistic Changes During Drug Treatment for Depression Using Tweets in
756 Spanish: Pairwise Comparison Study. *J Med Internet Res* **2020**, *22*,
757 doi:10.2196/20920.
- 758 76. Fornaro, M.; Anastasia, A.; Valchera, A.; Carano, A.; Orsolini, L.; Vellante, F.;
759 Rapini, G.; Olivieri, L.; Natale, S. Di; Perna, G.; et al. The FDA “Black Box”
760 Warning on Antidepressant Suicide Risk in Young Adults: More Harm Than
761 Benefits? *Front Psychiatry* **2019**, *10*, doi:10.3389/FPSYT.2019.00294.
- 762 77. Sharma, A.; Guski, L.S.; Freund, N.; Gøtzsche, P.C. Suicidality and Aggression
763 during Antidepressant Treatment: Systematic Review and Meta-Analyses Based
764 on Clinical Study Reports. *BMJ* **2016**, *352*, doi:10.1136/BMJ.l65.
- 765 78. Braun, C.; Bschor, T.; Franklin, J.; Baethge, C. Suicides and Suicide Attempts
766 during Long-Term Treatment with Antidepressants: A Meta-Analysis of 29
767 Placebo-Controlled Studies Including 6,934 Patients with Major Depressive
768 Disorder. *Psychother Psychosom* **2016**, *85*, 171–179, doi:10.1159/000442293.
- 769 79. Orsolini, L.; Latini, R.; Pompili, M.; Serafini, G.; Volpe, U.; Vellante, F.; Fornaro,
770 M.; Valchera, A.; Tomasetti, C.; Fraticelli, S.; et al. Understanding the Complex of
771 Suicide in Depression: From Research to Clinics. *Psychiatry Investig* **2020**, *17*,
772 207, doi:10.30773/PI.2019.0171.
- 773 80. Hengartner, M.P.; Amendola, S.; Kaminski, J.A.; Kindler, S.; Bschor, T.; Plöderl,
774 M. Suicide Risk with Selective Serotonin Reuptake Inhibitors and Other New-
775 Generation Antidepressants in Adults: A Systematic Review and Meta-Analysis
776 of Observational Studies. *J Epidemiol Community Health (1978)* **2021**, *75*, 523–
777 530, doi:10.1136/JECH-2020-214611.
- 778 81. Gunnell, D.; Saperia, J.; Ashby, D. Selective Serotonin Reuptake Inhibitors
779 (SSRIs) and Suicide in Adults: Meta-Analysis of Drug Company Data from
780 Placebo Controlled, Randomised Controlled Trials Submitted to the MHRA’s
781 Safety Review. *BMJ : British Medical Journal* **2005**, *330*, 385,
782 doi:10.1136/BMJ.330.7488.385.
- 783 82. Li, K.; Zhou, G.; Xiao, Y.; Gu, J.; Chen, Q.; Xie, S.; Wu, J. Risk of Suicidal
784 Behaviors and Antidepressant Exposure Among Children and Adolescents: A
785 Meta-Analysis of Observational Studies. *Front Psychiatry* **2022**, *13*,
786 doi:10.3389/FPSYT.2022.880496.

- 787 83. Du, J.; Zhang, Y.; Luo, J.; Jia, Y.; Wei, Q.; Tao, C.; Xu, H. Extracting Psychiatric
788 Stressors for Suicide from Social Media Using Deep Learning. *BMC Med Inform*
789 *Decis Mak* **2018**, *18*, doi:10.1186/S12911-018-0632-8.
- 790 84. Safa, R.; Bayat, P.; Moghtader, L. Automatic Detection of Depression Symptoms
791 in Twitter Using Multimodal Analysis. *J Supercomput* **2022**, *78*, 4709,
792 doi:10.1007/S11227-021-04040-8.
- 793 85. Fava, G.A.; Gatti, A.; Belaise, C.; Guidi, J.; Offidani, E. Withdrawal Symptoms
794 after Selective Serotonin Reuptake Inhibitor Discontinuation: A Systematic
795 Review. *Psychother Psychosom* **2015**, *84*, 72–81, doi:10.1159/000370338.
- 796 86. Montejo-Gonzalez, A.L.; Liorca, G.; Izquierdo, J.A.; Ledesma, A.; Bousono, M.;
797 Calcedo, A.; Carrasco, J.L.; Ciudad, J.; Daniel, E.; de la Gandara, J.; et al. SSRI-
798 Induced Sexual Dysfunction: Fluoxetine, Paroxetine, Sertraline, and
799 Fluvoxamine in a Prospective, Multicenter, and Descriptive Clinical Study of 344
800 Patients. *J Sex Marital Ther* **1997**, *23*, 176–194,
801 doi:10.1080/00926239708403923.
- 802 87. Hensley, P.L.; Nurnberg, H.G. SSRI Sexual Dysfunction: A Female Perspective.
803 *J Sex Marital Ther* **2002**, *28 Suppl 1*, 143–153,
804 doi:10.1080/00926230252851267.
- 805 88. Rosen, R.C.; Lane, R.M.; Menza, M. Effects of SSRIs on Sexual Function: A
806 Critical Review. *J Clin Psychopharmacol* **1999**, *19*, 67–85,
807 doi:10.1097/00004714-199902000-00013.
- 808 89. Ben-Sheetrit, J.; Hermon, Y.; Birkenfeld, S.; Gutman, Y.; Csoka, A.B.; Toren, P.
809 Estimating the Risk of Irreversible Post-SSRI Sexual Dysfunction (PSSD) Due to
810 Serotonergic Antidepressants. *Ann Gen Psychiatry* **2023**, *22*,
811 doi:10.1186/S12991-023-00447-0.
- 812 90. Saleh, R.; Majzoub, A.; Abu El-Hamd, M. An Update on the Treatment of
813 Premature Ejaculation: A Systematic Review. *Arab J Urol* **2021**, *19*, 281–302,
814 doi:10.1080/2090598X.2021.1943273.
- 815 91. Sathianathan, N.J.; Hwang, E.C.; Mian, R.; Bodie, J.A.; Soubra, A.; Lyon, J.A.;
816 Sultan, S.; Dahm, P. Selective Serotonin Re-Uptake Inhibitors for Premature
817 Ejaculation in Adult Men. *Cochrane Database Syst Rev* **2021**, *3*,
818 doi:10.1002/14651858.CD012799.PUB2.
- 819 92. Singh, J.B.; Daly, E.J.; Mathews, M.; Fedgchin, M.; Popova, V.; Hough, D.;
820 Drevets, W.C. Approval of Esketamine for Treatment-Resistant Depression.
821 *Lancet Psychiatry* **2020**, *7*, 232–235, doi:10.1016/S2215-0366(19)30533-4.
- 822 93. Wang, S.; Bian, L.; Yin, Y.; Guo, J. Targeting NMDA Receptors in Emotional
823 Disorders: Their Role in Neuroprotection. *Brain Sci* **2022**, *12*,
824 doi:10.3390/BRAINSCI12101329.
- 825 94. Gonda, X.; Dome, P.; Neill, J.C.; Tarazi, F.I. Novel Antidepressant Drugs: Beyond
826 Monoamine Targets. *CNS Spectr* **2023**, *28*, 6–15,
827 doi:10.1017/S1092852921000791.
- 828 95. Vasiliu, O. Esketamine for Treatment-resistant Depression: A Review of Clinical
829 Evidence (Review). *Exp Ther Med* **2023**, *25*, doi:10.3892/ETM.2023.11810.

- 830 96. Borentain, S.; Desai, P.; Fu, D.J.; Nancy Chen, L.; Lane, R.; Mathews, M.;
831 Canuso, C.M. Commentary on Cochrane Review: "Ketamine and Other
832 Glutamate Receptor Modulators for Depression in Adults with Unipolar Major
833 Depressive Disorder." *J Psychopharmacol* **2023**, *37*, 836–844,
834 doi:10.1177/02698811221123046.
- 835 97. Reif, A.; Bitter, I.; Buyze, J.; Cebulla, K.; Frey, R.; Fu, D.-J.; Ito, T.; Kambarov, Y.;
836 Llorca, P.-M.; Oliveira-Maia, A.J.; et al. Esketamine Nasal Spray versus
837 Quetiapine for Treatment-Resistant Depression. *N Engl J Med* **2023**, *389*, 1298–
838 1309, doi:10.1056/NEJM0A2304145.
- 839 98. Faisant, S.; Crublet, P.; Bellay, R.; Langrée, B.; Marie, N.; Rojo-Bouton, M.;
840 Vadukapuram, R.; Trivedi, C.; Mansuri, Z.; Shah, K.; et al. Early Real-Life
841 Evaluation of the Efficacy of Esketamine in Resistant Depressive Disorder.
842 *European Psychiatry* **2022**, *65*, S554, doi:10.1192/J.EURPSY.2022.1417.
- 843 99. Mahase, E. Esketamine for Treatment Resistant Depression Is Not
844 Recommended by NICE. *BMJ* **2020**, *368*, m329, doi:10.1136/BMJ.M329.
- 845 100. Ng, Q.X.; Lim, Y.L.; Ong, C.; New, S.; Fam, J.; Liew, T.M. Hype or Hope?
846 Ketamine for the Treatment of Depression: Results from the Application of Deep
847 Learning to Twitter Posts from 2010 to 2023. *Front Psychiatry* **2024**, *15*,
848 doi:10.3389/FPSYT.2024.1369727/FULL.
- 849 101. Palamar, J.J.; Wilkinson, S.T.; Carr, T.H.; Rutherford, C.; Cottler, L.B. Trends in
850 Illicit Ketamine Seizures in the US From 2017 to 2022. *JAMA Psychiatry* **2023**,
851 *80*, 750–751, doi:10.1001/JAMAPSYCHIATRY.2023.1423.
- 852 102. Español de las Drogas las Adicciones, O. INFORME 2022 Alcohol, Tabaco y
853 Drogas Ilegales En España E N C U E S T A S O B R E U S O D E D R O G A S
854 E N E N S E Ñ A N Z A S S E C U N D A R I A S E N E S P A Ñ A (E S T U D E S
855), 1 9 9 4 - 2 0 2 1.
- 856 103. Palamar, J.J. Tusi: A New Ketamine Concoction Complicating the Drug
857 Landscape. *Am J Drug Alcohol Abuse* **2023**, *49*, 546–550,
858 doi:10.1080/00952990.2023.2207716.
- 859 104. Carabot, F.; Donat-Vargas, C.; Santoma-Vilaclara, J.; Ortega, M.A.; García-
860 Montero, C.; Fraile-Martínez, O.; Zaragoza, C.; Monserrat, J.; Alvarez-Mon, M.;
861 Alvarez-Mon, M.A. Exploring Perceptions About Paracetamol, Tramadol, and
862 Codeine on Twitter Using Machine Learning: Quantitative and Qualitative
863 Observational Study. *J Med Internet Res* **2023**, *25*, doi:10.2196/45660.
- 864 105. Carabot, F.; Fraile-Martínez, O.; Donat-Vargas, C.; Santoma, J.; Garcia-Montero,
865 C.; da Costa, M.P.; Molina-Ruiz, R.M.; Ortega, M.A.; Alvarez-Mon, M.; Alvarez-
866 Mon, M.A. Understanding Public Perceptions and Discussions on Opioids
867 Through Twitter: Cross-Sectional Infodemiology Study. *J Med Internet Res* **2023**,
868 *25*, doi:10.2196/50013.
- 869 106. Grabski, M.; Waldron, J.; Freeman, T.P.; van Laar, M.; Curran, H.V. Is Approving
870 Esketamine as an Antidepressant for Treatment Resistant Depression Associated with
871 Recreational Use and Risk Perception of Ketamine? Results from a Longitudinal and
872 Cross-Sectional Survey in Nightlife Attendees. *Int J Drug Policy* **2022**, *102*,
873 doi:10.1016/J.DRUGPO.2022.103612.

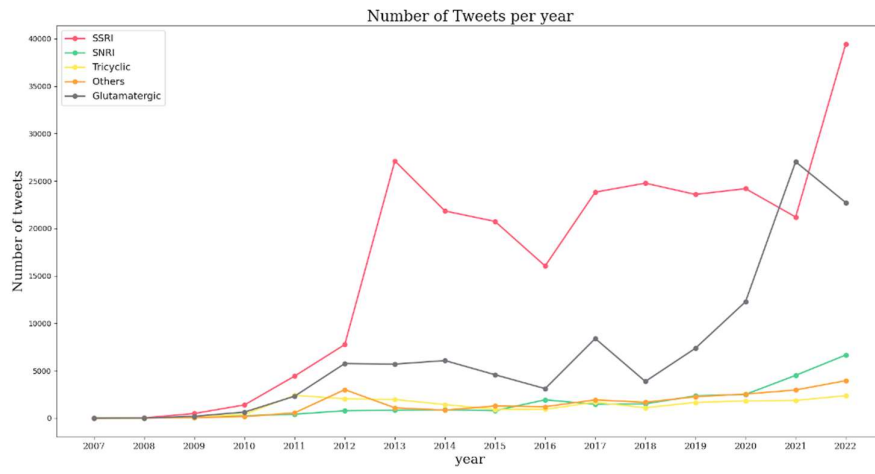
874 Figure 1



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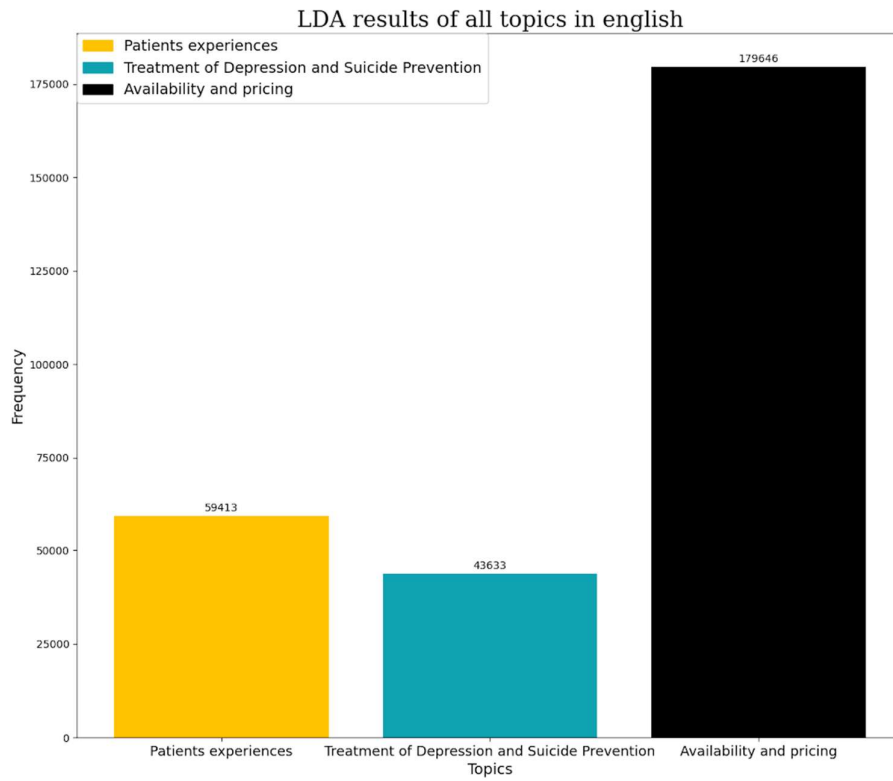
877 Figure 2



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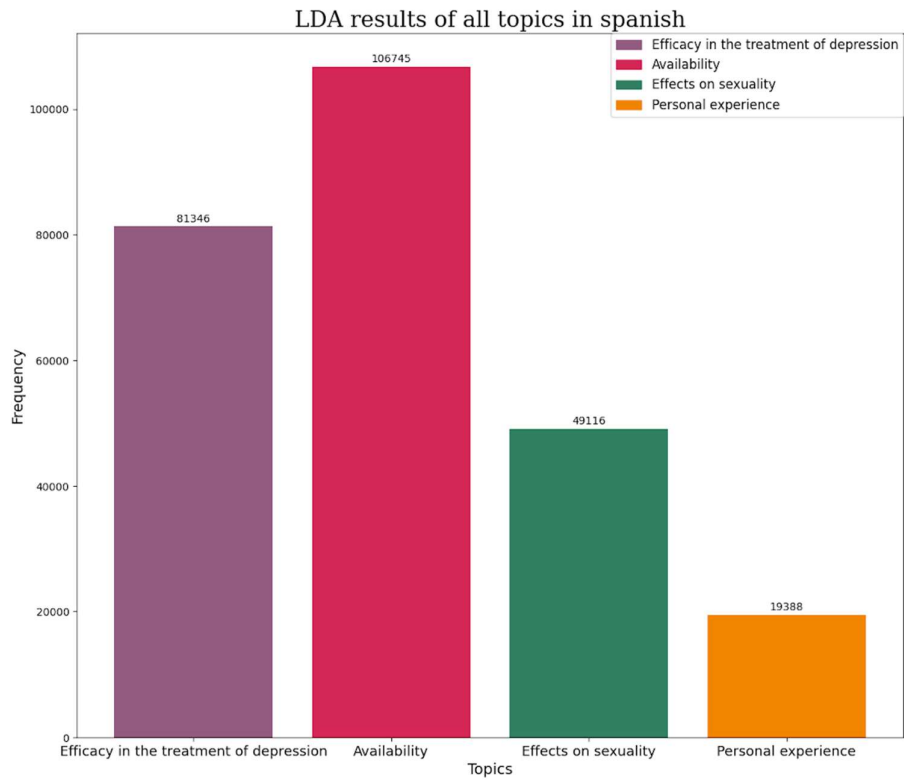
880 Figure 3



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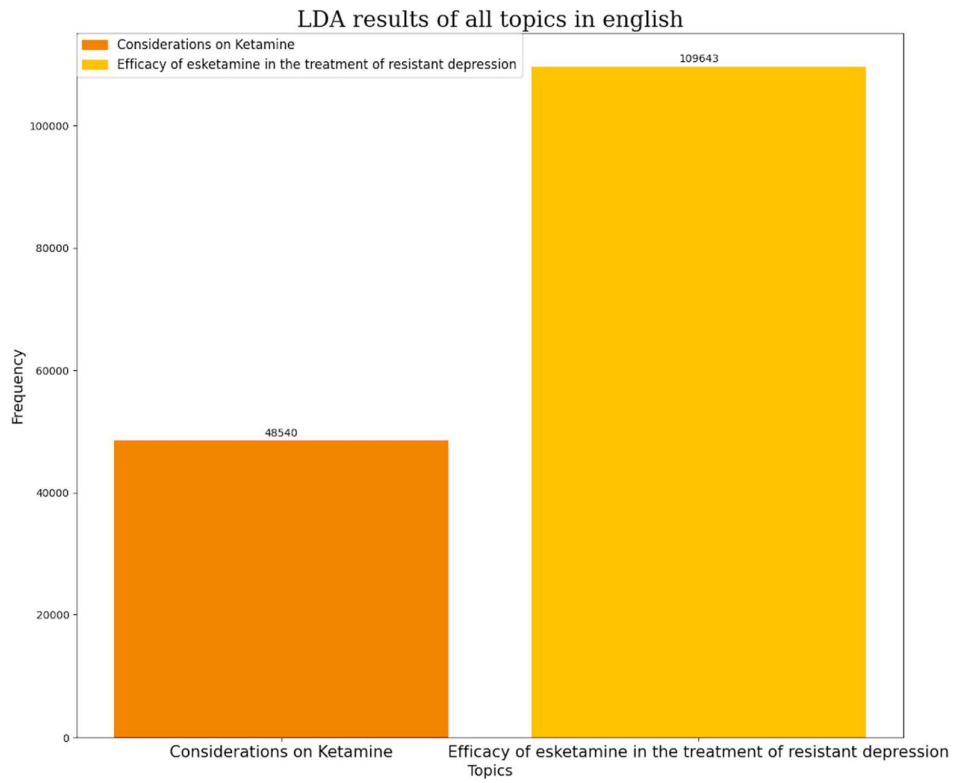
883 Figure 4



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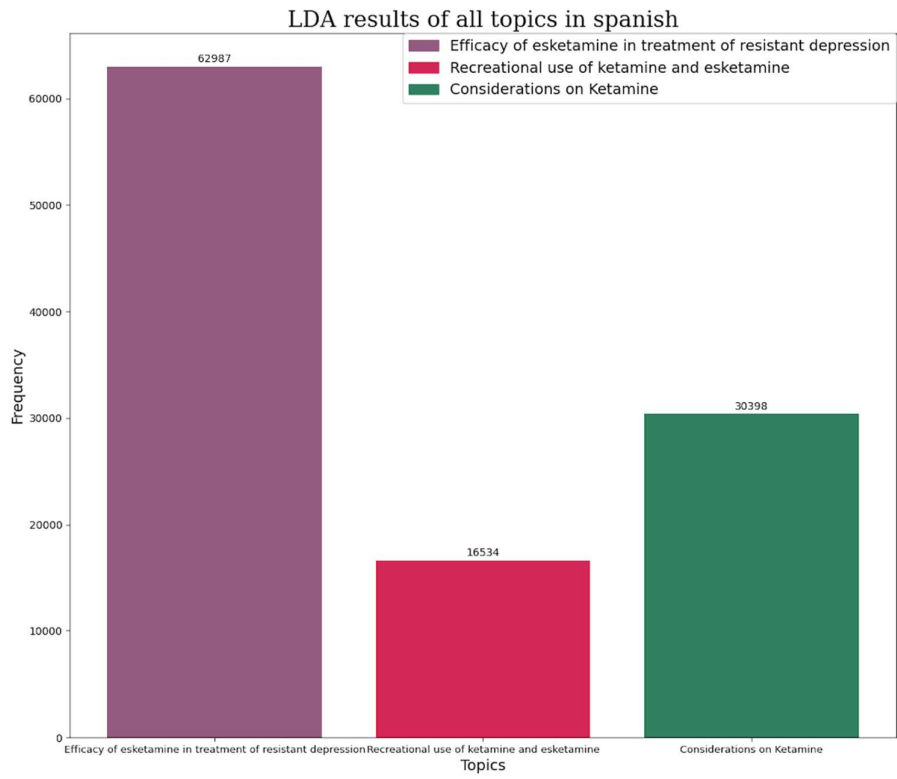
886 Figure 5



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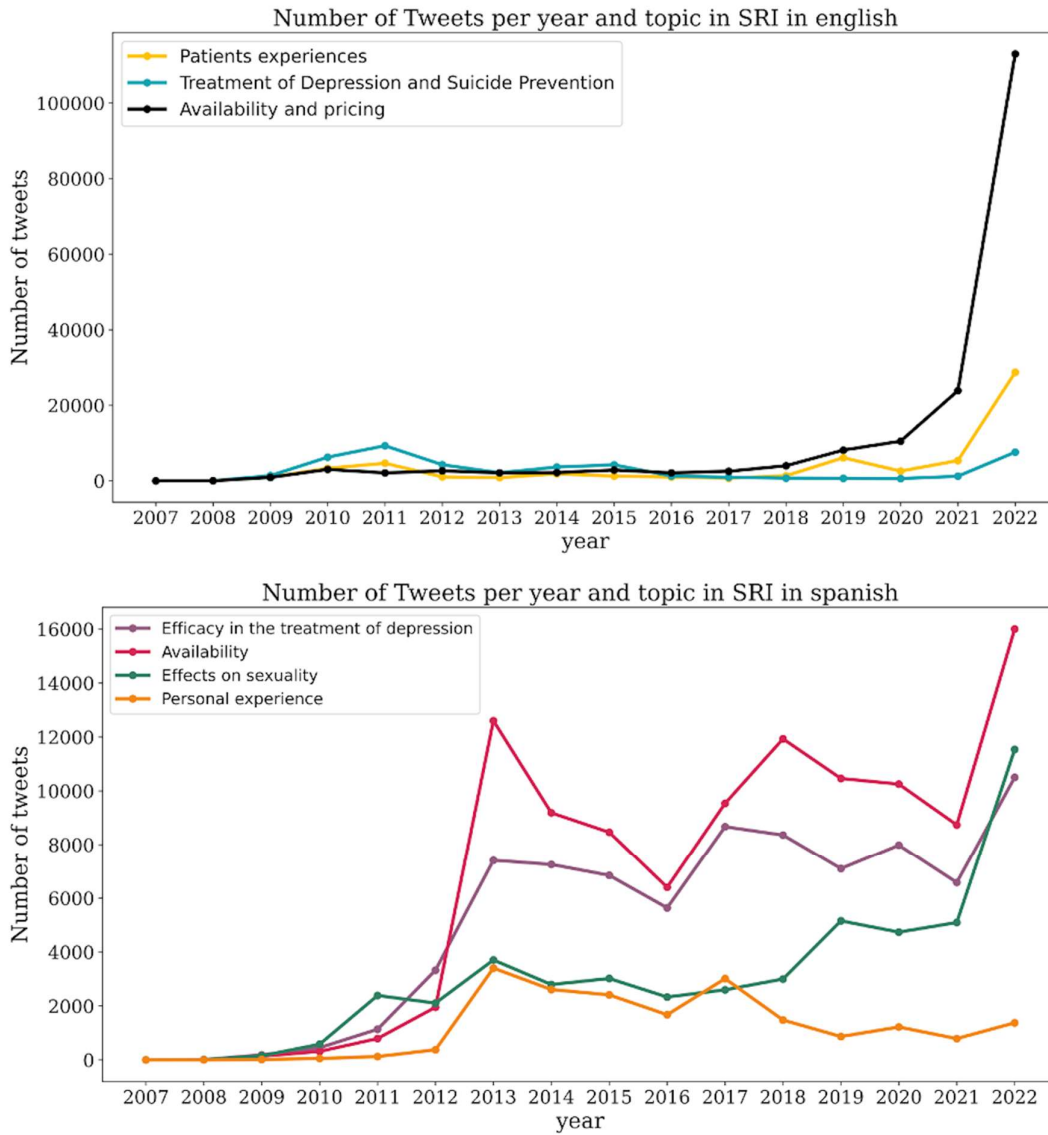
889 Figure 6



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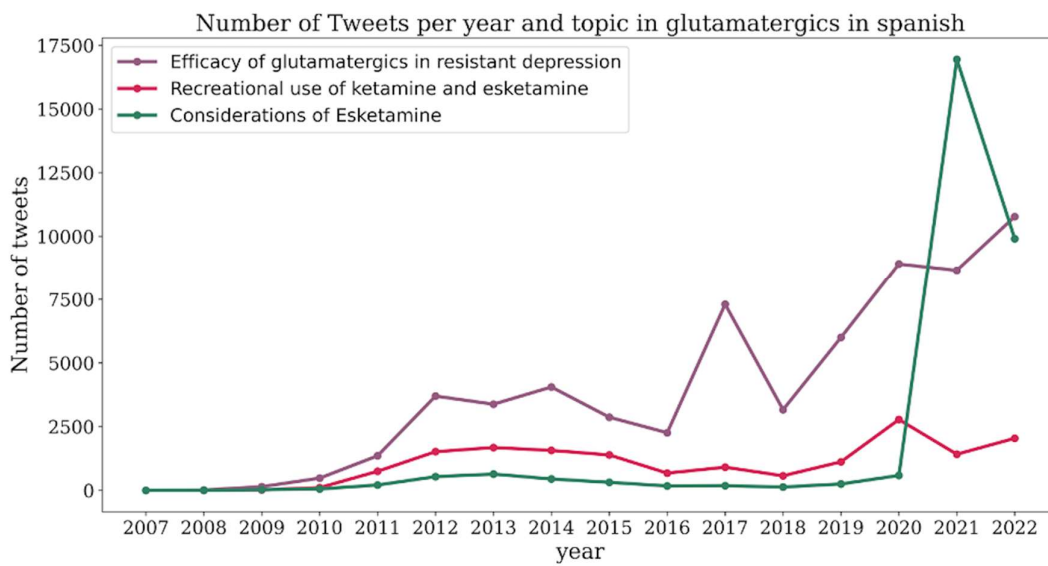
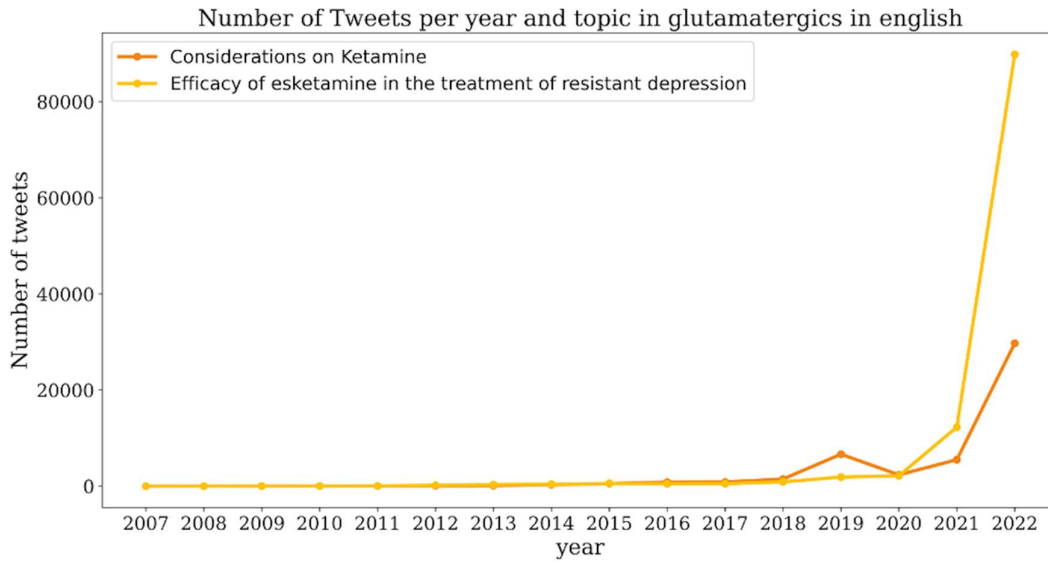
892 Figure 7



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895 Figure 8



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898 Figure 9

A

Topic comparison for SSRI meds in english database



B

Topic comparison for SSRI meds in spanish database



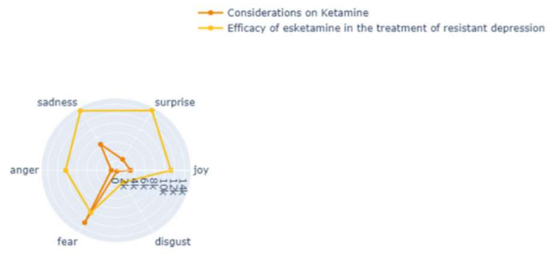
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901 Figure 10

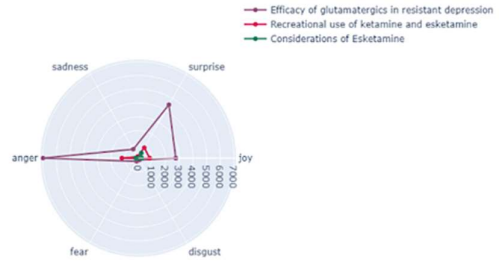
A

Topic comparison for glutamatergic meds in english database



B

Topic comparison for glutamatergic meds in spanish database



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